CLAIMS

1. A microcapsule for the modified release of at least one AP with low water solubility, *with the exclusion of blood glucose-lowering agents*, intended to be administered orally and of the type of those:

- each consisting of a core comprising at least one active principle and of a coating film applied onto the core and controlling the modified release of the AP(s),
- the mean diameter of which is less than 1000 microns, preferably between 800 and 50 microns, and even more preferably between 600 and 100 microns,
- in which the coating film of each microcapsule contains the following components:
  - → -I-- at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids,
  - → -II-- at least one water-soluble polymer (P2),
  - → -III- at least one plasticizer (PL),
  - → -IV- and, optionally, at least one lubricating surfactant (TA);

with the exclusion of coating films consisting of enteric compositions and of coating films having the composition below:

1 - at least one film-forming polymer (P1) insoluble in the fluids of the tract, present in a proportion of 50 to 90, preferably 50 to 80% by weight on a dry basis relative to the total mass of the coating composition and consisting of at least one water-insoluble derivative of cellulose, i.e. ethylcellulose and/or cellulose acetate;

2 - at least one nitrogenous polymer (P2) present in a proportion of 2 to 25, preferably 5 to 15% by weight on a dry basis relative to the total mass of the coating composition and consisting of at

least one polyacrylamide and/or one poly-N-vinylamide and/or one poly(N-vinyl lactam), i.e. polyacrylamide and/or polyvinylpyrrolidone;

3 - at least one plasticizer present in a proportion of 2 to 20, preferably 4 to 15% by weight on a dry basis relative to the total mass of the coating composition and consisting of at least one of the following compounds: glyceryl esters, phthalates, citrates, sebacates, cetyl alcohol esters, castor oil, salicylic acid and cutin;

4 - and at least one surfactant and/or lubricant, present in a proportion of 2 to 20, preferably 4 to 15% by weight on a dry basis relative to the total mass of the coating composition and chosen from anionic surfactants, i.e. alkali metal salts or alkaline-earth metal salts of fatty acids, stearic acid and/or oleic acid being preferred, and/or from nonionic surfactants, i.e. polyoxyethylenated sorbitan esters and/or polyoxyethylenated castor oil derivatives, and/or from lubricants such as calcium stearate, magnesium stearate, aluminum stearate or zinc stearate, or such as sodium stearyl fumarate and/or glyceryl behenate; it being possible for said agent to comprise just one or a mixture of the abovementioned products;

characterized:

- in that their coating film represents at least 3% dry weight/dry weight, preferably at least 5% dry weight/dry weight of their total mass,
- and in that the components P1, P2 and PL of the coating film satisfy the following characteristics:
  - mass fraction by dry weight of P1 relative to the total mass of the coating of between 40 and 90%, and preferably of between 50 and 80%;
  - mass fraction by dry weight P2/P1+P2 of

between 15 and 60%, and preferably of between 15 and 55%;

- mass fraction by dry weight PL/P1+PL of between 1 and 30%, and preferably of between 5 and 25%.

2. The microcapsule as claimed in claim 1, without the exclusion relating to blood glucose-lowering agents and without the exclusion relating to coating films consisting of enteric compositions and to coating films having the composition 1, 2, 3 and 4 as defined in claim 1.

3. The microcapsule as claimed in claim 1 or 2, characterized in that the coating film comprises component TA in a proportion of 2 and 20%, and preferably of between 4 and 15% of the total mass of the dry coating.

4. The microcapsule as claimed in any one of claims 1 to 3, characterized in that P1 is selected from the group of products below:

- water-insoluble derivatives of cellulose, preferably ethylcellulose and/or cellulose acetate,
- acrylic derivatives,
- poly(vinyl acetates),
- and mixtures thereof.

5. The microcapsule as claimed in any of one of claims 1 to 4, characterized in that P2 is selected from the group of products below:

- water-soluble derivatives of cellulose,
- polyacrylamides,
- poly-N-vinylamides,
- poly(N-vinyl lactams),
- polyvinyl alcohols (PVAs),
- polyoxyethylenes (POEs),
- polyvinylpyrrolidones (PVPs) (the latter being preferred),
- and mixtures thereof.

6. The microcapsule as claimed in any one of claims 1 to 5, characterized in that PL is selected

from the group of products below:

- glycerol and esters thereof, preferably from the following subgroup:
  acetylated glycerides, glyceryl monostearate, glyceryl triacetate, glyceryl tributyrate,
- phthalates, preferably from the following subgroup:
  dibutyl phthalate, diethyl phthalate, dimethyl phthalate, dioctyl phthalate,
- citrates, preferably from the following subgroup:
  acetyl tributyl citrate, acetyl triethyl citrate, tributyl citrate, triethyl citrate,
- sebacates, preferably from the following subgroup:
  diethyl sebacate, dibutyl sebacate,
- adipates,
- azelates,
- benzoates,
- plant oils,
- fumarates, preferably diethyl fumarate,
- malates, preferably diethyl malate,
- oxalates, preferably diethyl oxalate,
- succinates, preferably dibutyl succinate,
- butyrates,
- cetyl alcohol esters,
- salicylic acid,
- triacetin,
- malonates, preferably diethyl malonate,
- cutin,
- castor oil (this being particularly preferred),
- and mixtures thereof.

7. The microcapsule as claimed in any one of claims 1 to 6, characterized in that TA is selected from the group of products below:

- anionic surfactants, preferably from the subgroup of alkali metal salts or alkaline-

earth metal salts of fatty acids, stearic acid and/or oleic acid being preferred,

- and/or nonionic surfactants, preferably from the following subgroup:
  - o polyoxyethylenated oils, preferably polyoxyethylenated hydrogenated castor oil,
  - o polyoxyethylene-polyoxypropylene copolymers,
  - o polyoxyethylenated sorbitan esters,
  - o polyoxyethylenated castor oil derivatives,
  - o stearates, preferably calcium stearate, magnesium stearate, aluminum stearate or zinc stearate,
  - o stearyl fumarates, preferably sodium stearyl fumarate,
  - o glyceryl behenate,
  - o and mixtures thereof.

8. The microcapsule as claimed in any one of claims 1 to 7, characterized in that the APs with low solubility are chosen from at least one of the major varieties of active substances below:
antiulcer agents, antidiabetic agents, anticoagulants, antithrombics, blood lipid-lowering agents, antiarrhythmics, vasodilators, antiangina agents, antihypertensives, vasoprotective agents, fertility promoters, inducers and inhibitors of uterine labor, contraceptives, antibiotics, antifungal agents, antiviral agents, anticancer agents, anti-inflammatories, analgesics, antiepileptics, antiparkinsonian agents, neuroleptics, hypnotics, anxiolytics, psychostimulants, antimigraine agents, antidepressives, antitussives, antihistamines or antiallergic agents.

9. The microcapsule as claimed in claim 8 characterized in that the AP(s) with low solubility is (are) chosen from the following compounds: prazosine, acyclovir, nifedipine, naproxen, ibuprofen, ketoprofen, fenoprofen, indomethacine, diclofenac, sulpiride, terfenadine, carbamazepine, fluoxetine, alprazolam, famotidine, ganciclovir, spironolactone,

acetylsalicyclic acid, quinidine, morphine, amoxicillin, paracetamol, metoclopramide, verapamil and mixtures thereof.

10. A medicinal product comprising the microcapsules as claimed in any one of claims 1 to 9.

11. The medicinal product as claimed in claim 10, characterized in that it is in solid form, preferably: tablet, gelatin capsule or powder, or in liquid form, preferably: an aqueous suspension.

12. The use of microcapsules for the modified release of at least one AP with low water solubility, *with the exclusion of blood glucose-lowering agents,* intended to be administered orally, these microcapsules having the following characteristics:

- they each consist of a core comprising at least one active principle and of a coating film applied onto the core and controlling the prolonged release of the AP(s),
- their mean diameter is less than 1000 microns, preferably between 800 and 50 microns, and even more preferably between 600 and 100 microns,
- their coating film contains the following components:
  - → -I-- at least one film-forming polymer (P1) insoluble in gastrointestinal tract fluids,
  - → -II-- at least one water-soluble polymer (P2),
  - → -III- at least one plasticizer (PL),
  - → -IV- and, optionally, at least one lubricating surfactant (TA);

  components P1, P2 and Pl of the coating film satisfying the following characteristics:
  - ⇨ mass fraction by dry weight of P1 relative to the total mass of the coating of between 40 and 90%, and preferably of between 50 and 80%;
  - ⇨ mass fraction by dry weight P2/P1+P2 of

between 15 and 60%, and preferably of between 15 and 55%;

⇨ mass fraction by dry weight PL/P1+PL of between 1 and 30%, and preferably of between 5 and 25%;

- and this coating film represents at least 4% w/w, preferably at least 5% w/w of their total mass;

with the exclusion of coating films consisting of enteric compositions and of coating films having the composition below:

1 - at least one film-forming polymer (P1) insoluble in the fluids of the tract, present in a proportion of 50 to 90, preferably 50 to 80% by weight on a dry basis relative to the total mass of the coating composition and consisting of at least one water-insoluble derivative of cellulose, i.e. ethylcellulose and/or cellulose acetate;

2 - at least one nitrogenous polymer (P2) present in a proportion of 2 to 25, preferably 5 to 15% by weight on a dry basis relative to the total mass of the coating composition and consisting of at least one polyacrylamide and/or one poly-N-vinyl-amide and/or one poly(N-vinyl lactam), i.e. polyacrylamide and/or polyvinylpyrrolidone;

3 - at least one plasticizer present in a proportion of 2 to 20, preferably 4 to 15% by weight on a dry basis relative to the total mass of the coating composition and consisting of at least one of the following compounds: glyceryl esters, phthalates, citrates, sebacates, cetyl alcohol esters, castor oil, salicylic acid and cutin;

4 - and at least one surfactant and/or lubricant, present in a proportion of 2 to 20, preferably 4 to 15% by weight on a dry basis relative to the total mass of the coating composition and chosen from anionic surfactants, i.e. alkali metal salts or alkaline-earth metal salts of fatty acids, stearic acid and/or oleic acid being preferred,

and/or from nonionic surfactants, i.e. polyoxyethylenated sorbitan esters and/or polyoxyethylenated castor oil derivatives, and/or from lubricants such as calcium stearate, magnesium stearate, aluminum stearate or zinc stearate, or such as sodium stearyl fumarate and/or glyceryl behenate; it being possible for said agent to comprise just one or a mixture of the abovementioned products;

for producing a medicinal product based on at least one AP with low solubility which can be administered orally, which can be readily swallowed, and which is released in vivo in a controlled, prolonged and, optionally, delayed manner.

13. The use as claimed in claim 12, without the exclusion relating to blood glucose-lowering agents and without the exclusion relating to coating films consisting of enteric compositions and to coating films having the composition 1, 2, 3 and 4 as defined in claim 12.